Attorney's Docket No.: 16601-021US1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Samuel Weiss	Art Unit	: 1636
Serial No.	: 10/523,253	Examiner	: Laura L. McGillem
Filed	: January 26, 2005	Conf. No.	: 8661
Title	: OLIGODENDROCYTE PRODUCTION FROM MULTIPOTENT NEURAL STEM CELLS		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132 BY SAMUEL WEISS

I, Samuel Weiss, Ph.D., pursuant to 37 C.F.R. § 1.132, declare the following:

1. I am the Director of the Hotchkiss Brain Institute and the Alberta Heritage Foundation for Medical Research Scientist in the Departments of Cell Biology & Anatomy and Pharmacology & Therapeutics at the University of Calgary, Faculty of Medicine, Calgary, Alberta. I have been engaged in neurobiochemistry research for over 20 years.

2. I am the inventor of the claimed invention described in the patent application captioned above ("the patent application").

3. I have read and understood the Office Action in the above case dated October 15, 2007, as well as the references cited and discussed in this case.

4. I have been informed that a "person of ordinary skill in the art" is one who is presumed to be aware of all pertinent art, thinks along conventional wisdom in the art, and is not one who undertakes to innovate. Persons of ordinary skill could conceivably include one with knowledge of the scientific literature available on or before January 26, 2005 concerning neural stem cell differentiation and proliferation, and the use of factors to impact or direct neural stem cell differentiation and proliferation. Preferably, a "person of ordinary skill in the art" would have a scientific background such as a Bachelor's degree or higher in biological sciences and have familiarity with techniques involved in molecular biology and neural stem cell technologies.

5. The Office Action states that my previously submitted Declaration showing that GM-CSF increases the production of oligodendrocytes in a mouse model "does not provide sufficient evidence for producing oligodendrocytes comprising contacting multipotent neural stem cells in any other mammal other than a rodent (i.e. human) using any other oligodendrocyte promoting factor." Office Action mailed October 15, 2007 at p. 5. As outlined in items 6-8 below, those of skill in the art recognize that mouse models are accepted models for demonstrating neural stem cell differentiation and proliferation and that these models are widely used.

6. Mouse models are widely used by those of skill in the art to research properties of the human central nervous system (CNS) and treatment of CNS diseases or conditions. The following are but a few example of scientific papers published recently that use mouse models to research properties of the CNS and CNS diseases and conditions:

a) Anne Comi *et al.*, *A new model of stroke and ischemic seizures in the immature mouse*, Pediatric Neurology (2004) 31: 254-257 (mouse model of brain injury due to stroke).

b) Brian K. Kaspar *et al.*, *Retrograde viral delivery of IGF-1 prolongs survival in a mouse ALS model*, Science (2003) 301: 839-42 (mouse model to demonstrate delivery of IGF-1 and GDNF to the spinal cord by AAV vectors after intramusclar injection).

c) Dong-Eog Kim *et al.*, *Neural stem cell transplant survival in brains of mice: assessing the effect of immunity and ischemia by using real-time bioluminexcent imaging*, Radiology (2006) 241: 822-30 (mouse model to monitor *in vivo* response of transplanted neural progenitor cells).

d) Alysson R. Muotri *et al.*, *Development of functional human embryonic stem cell-derived neurons in mouse brain*, PNAS (2005) 102: 18644-48 (mouse model showing integration of human cells into the mouse brain and indicating that the

study "reveals the conservation and recognition of common signals for neural differentiation throughout mammalian evolution").

c) Weihong Pan *et al.*, *Stroke upregulates TNFα transport across the blood-brain barrier*, Exp. Neurology (2006) 198: 222-33 (mouse model of cerebral ischemia and reperfusion to determine TNFα transfer across the blood brain barrier).

f) Gwen S. Scott *et al.*, *Uric acid protects against secondary damage after spinal cord injury*, PNAS (2005) 102: 3483-88 (mouse model of spinal cord injury to evaluate uric acid protection after injury).

7. I commonly use mouse models in my own research regarding neural stem cell properties as evidenced by the following scientific papers:

a) Gloria K. Mak *et al.*, *Male pheromone-stimulated neurogenesis in the adult female brain: possible role in mating behavior*, Nature Neuroscience (2007) 10: 1003-1011 (mouse model to investigate pheromone-stimulated neurogenesis).

b) Shigeki Ohta *et al.*, *Pituitary Adenylate Cyclase-Activating Polypeptide regulates forebrain neural stem cells and neurogenesis in vitro and in vivo*, J. Neuroscience Res. (2006) 84: 1177-1186 (mouse model to investigate whether PACAP promotes neural stem cell proliferation, self-renewal, and neurogenesis).

c) Tetsuro Shingo *et al.*, *Pregnancy-stimulated neurogenesis in the adult female forebrain mediated by prolactin*, Science (2003) 299: 117-120 (mouse model to investigate the effects of prolactin on neurogenesis noting that "[b]ehavioral studies in rodents and primates, which show virtually identical patterns of adult olfactory neurogenesis, will serve to address these intriguing possibilities").

d) Tetsuro Shingo *et al.*, *Erythropoietin regulates the in vitro and in vivo production of neuronal progenitors by mammalian forebrain neural stem cells*, J.

Neuroscience (2001) 21: 9733-9743 (mouse model to investigate the effects of EPO on the production of neural progenitor cells).

c) Takuya Shimazaki *et al.*, *The ciliary neurotrophic factor/leukemia inhibitory factor/gp130 receptor complex operates in the maintenance of mammalian forebrain neural stem cells*, J. Neuroscience (2001) 21: 7642-7653 (mouse model to investigate whether CNTF supports the self-renewal of EGF-responsive neural stem cells).

8. As demonstrated by the above cited papers, mouse models for research into properties of the CNS, CNS diseases and conditions, and treatments are widely accepted. These models provide valuable tools in the screening and development of novel drugs for the treatment of CNS diseases and conditions.

9. While mouse models may not be able to predict with 100% accuracy the efficacy of compounds for the treatment of stem cell related diseases and conditions in humans, the models provide valuable information that may lead to novel treatments of neurologic diseases and conditions in humans.

10. The present specification and my earlier submitted declaration ("the First Weiss Declaration") provide *in vitro* and *in vivo* evidence that the claimed compounds promote oligodendrocyte production from neural stem cells. Specifically, the specification and the First Weiss Declaration demonstrate that GM-CSF promotes oligodendrocyte production from neural stem cells. Therefore, based on my knowledge and review of the specification and related literature, one of skill in the art would reasonably conclude that the claimed compounds promote oligodendrocyte production from neural stem cells based on the *in vitro* and *in vivo* data presented.

11. For the above reasons, based on my education and scientific experience, one of skill in the art would appreciate that, despite some drawbacks, mouse animal models are widely accepted as a tool to develop treatments of neurologic disorders.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: Jan. 10, 2008

Samuel Weiss, Ph.D.

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